

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Rajiv Shah, et al.

Title: METHOD FOR FORMULATING A GLUCOSE OXIDASE ENZYME WITH A DESIRED PROPERTY OR PROPERTIES AND A GLUCOSE OXIDASE ENZYME WITH THE DESIRED PROPERTY

Appl. No.: 10/035,918

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Examiner: Yong D. Pak

Art Unit: 1652

Confirmation No.: 2208

REPLY BRIEF UNDER 37 CFR 1.193

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Commissioner for Patents
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Sir:

Applicant presents this Reply Brief in response to the Examiner's Answer mailed on March 10, 2009.

In the Examiner's Answer, the rejections raised in the final Office Action dated June 27, 2008 were essentially repeated. Accordingly, Applicant's comments on pages 8-25 of the Appeal Brief filed September 23, 2008, address those rejections and are re-emphasized and incorporated herein by reference.

In addition, the Examiner's Answer includes a section (10) titled "Response to Argument." The present Reply Brief addresses comments included in that section (10) of the Examiner's Answer.

In that section of the Examiner's Answer, the Examiner acknowledges that Valdes et al. do not teach a method of producing a library of mutated glucose oxidase genes, but, instead teach another (different) process to "prevent the degradation of the enzyme using other chemical agents, or techniques" (emphasis added by Examiner), citing the left paragraph of Valdes, pg. 375. (Answer, pg. 11, ll. 6-10.)

The Examiner emphasizes Valdes et al.'s use of the word "techniques" in the portion of the above-quoted phrase stating "other chemical agents, or techniques." (Underline added for emphasis.) The Examiner's arguments appear to be based, at least in part, on the position that Valdes et al.'s reference to "techniques" is a general reference to any other technique and, such would have led one of ordinary skill in the art to employ techniques as taught by Cherry for generating mutants having resistance to chemicals.

"Examiner is taking the position that one having ordinary skill in the art would have concluded that peroxide degradation of glucose oxidase may be prevented by using chemical agents, as suggested by Valdes et al. or to use other 'techniques,' such as generating glucose oxidase mutants that are resistant to peroxide since methods of generating mutants having resistance to chemicals are known in the art, as taught by Cherry et al." (Answer, pg. 11, ll. 13-18.)

First, a general reference to "techniques" would not have taught or suggested a mutation generating process. The term "techniques" does not, itself teach or suggest any specific process, much less a process for making a dye-bleaching reagent in a detergent for washing clothes, as described by Cherry et al.

Second, Valdes et al. describes specific techniques in the paragraphs immediately following the phrase "other chemical agents, or techniques." In particular, in the next paragraph (indeed, the next sentence) following their reference to "other chemical agents, or techniques," Valdes et al. describe the addition of catalase chemical agent additives. Then in the very next paragraph, Valdes et al. describe other techniques for a long term remedy (thus defining what was meant by the term "techniques" in the phrase "other chemical agents, or techniques"). In particular, Valdes et al. describe the following techniques:

“A long-term remedy of the degradation of GOD by H₂O₂ could be the immobilization and attachment of the enzyme to a support that deactivates H₂O₂, as it is being produced. Such a study was conducted by Cho [citing appendix reference 2 in the Valdes et al. article] ... In a study conducted by Carter [citing appendix reference 19], the best results were obtained with activated carbon, impregnated with ruthenium.” (Valdes et al., pg. 375, col. 1, l. 18 to col. 2, l. 4.)

Valdes et al.’s reference to “other chemical agents, or techniques” is, thus, immediately followed by their description of chemical agents and techniques. One of ordinary skill in the art would clearly have been taught by Valdes et al. toward the chemical agents and techniques described in the reference immediately after referring to “chemical agents, or techniques.” Furthermore, it is respectfully submitted that one of ordinary skill in the art would not have been led by Valdes et al.’s reference to “techniques,” to use processes employed in the manufacture of detergent for washing clothes (a field far outside the field of endeavor of the Valdes et al. reference).

Thus, Valdes et al. directs the reader to specific techniques (immediately after referring to “techniques”), in which an enzyme is immobilized, attached to a support material that deactivates H₂O₂ as it is produced (as described in specific studies by Cho and Carter cited by Valdes et al.). One of ordinary skill in the art would have had a specific definition of such “techniques” directly in the article. The Examiner has not provided an appropriate reason why one of ordinary skill in the art would have been motivated to employ different techniques than those actually described by Valdes et al., much less processes used in an unrelated field of endeavor (manufacturing detergent for washing clothes).

The Examiner’s focus on the term “techniques” in Valdes et al.’s phrase “other chemical agents, or techniques” takes that term out of context (and separates it from the sentences immediately following that phrase). One of ordinary skill in the art would not have read the term “techniques” alone and outside of the context in which Valdes et al. use that term. If Valdes et al. were read as a whole (without reading the one word “techniques” out of context), the reference to “techniques” would have been read in conjunction with the specific example techniques described in the text immediately after the use of the term.

Thus, Valdes et al. teach a specific approach (chemical additives or attaching to supports made of deactivating material) to address peroxide degradation, but the direction of that approach is away from the direction of the present invention. One of ordinary skill in the art, would have been taught by Valdes et al., consistent with the direction of the industry, to employ chemical agents or techniques (those chemical agents and techniques described immediately following Valdes et al.'s reference to chemical agents and techniques). The Examiner's focus on the term "techniques" alone is improper, in that it does not take into account the specific teachings of Valdes et al. and the direction of those of ordinary skill in the art at the time of the invention (as evidenced by the specific technique examples described by Valdes et al.).

Furthermore, Applicant has cited additional evidence of record (in addition to Valdes et al.) that shows that a direction taken by those of ordinary skill in the art was away from that of the present invention. In particular, conventional "additive" processes for removing or neutralizing peroxide (such as by adding an antioxidant or peroxidase to the glucose oxidase to break down peroxide or by coating the glucose oxidase enzyme with a protective coating), are described in U.S. Patent No. 6,689,265 to Heller et al. (Exhibit 1 to Applicant's Appeal Brief) and the article titled "Glucose ENFET doped with MnO₂ powder" by Yin et al.

Thus, both the Heller et al. patent and the Yin et al. article show that a direction taken by those skilled in the art was to provide additives or complex multi-layer sensor structures to remove hydrogen peroxide. These references, in addition to Valdes et al.'s express references to conventional uses of additives, show that those skilled in the art were attempting to address the peroxide production issue by removing or neutralizing peroxide with additives. The state and direction of the industry, as evidenced by Valdes et al., Heller et al. and Yin et al., was a wholly different direction than that taken by the present Applicants. Accordingly, evidence of record (including the primary reference relied upon by the Examiner) shows that skilled artisans were taking a direction different from (and away from) the present invention.

Without the present disclosure as a guide, one of ordinary skill in the art would not have found Valdes et al.'s discussion of the degradation of glucose oxidase as a prompt or suggestion to employ a mutation process for detergent as described Cherry et al. Instead, as noted above, one of ordinary skill in the art would have looked to conventional manners of removing peroxide,

such as additives for removing or neutralizing peroxide. Accordingly, the Examiner has not raised a *prima facie* case of obviousness over the Valdes et al. reference and has failed to show that one skilled in the art would have found any reason or motivation to look to and adopt a process entirely different from the direction of the industry, much less a process as described by Cherry (for making clothes washing detergent). The Examiner's reliance on the term "techniques" in the Valdes et al. reference is misplaced and does not remedy the lack of reason or motivation to depart from the direction of the industry (much less adopt processes used in making detergent for washing clothes). Accordingly, the rejections of 1, 3-8, 10-24 and 44-46 under 35 U.S.C. 103(a) are traversed and should be reversed..

Next, the Examiner argues that "the absence of alternatives of a solution (i.e., mutant glucose oxidase resistant to peroxide degradation) does not criticize, discredit, or otherwise discourage the solution claimed." (Answer, pg. 12, ll. 1-3.) However, the Examiner's argument ignores the fact that Valdes et al. teach a specific direction (an approach to peroxide degradation that involves using chemical additives or techniques of immobilizing and attaching the enzyme on a support that deactivates peroxide) that is away from the direction of the present invention. Valdes et al. (as well as other evidence of record, including the Heller et al. and Yin et al. references discussed above) show that the focus of the industry was directed away from the direction of the present invention.

Thus, it is true that Valdes et al. has an absence of a description of formulating an enzyme by mutating glucose oxidase to have a desired property. In addition, it cannot be ignored that Valdes et al. teach specific techniques, showing the direction taken by those in the biosensor enzyme industry at the time of the invention. Other references of record (e.g., Heller et al. and Yin et al.) also describe techniques that show the direction of that industry. Thus, there is more to Valdes et al. than the absence of a description of mutating glucose oxidase. The Examiner's argument does not properly consider Valdes et al.'s teachings (of adding deactivating chemical agents, or attaching an enzyme to a support made of deactivating material) and also does not properly consider the additional evidence of record showing direction of the industry at the time of the present invention.

The Examiner's argument that Valdes et al. does not teach away from the present invention, because Valdes et al. do not criticize, discredit or otherwise discourage the claimed solution, ignores the fact that Valdes et al do teach (and, thus encourages) a particular direction that is not the direction taken by the present invention. "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, . . . would be led in a direction divergent from the path that was taken by the applicant." *Tec Air, Inc. v. Denso Mfg. Mich. Inc.*, 192 F.3d 1353, 1360, 52 USPQ2d 1294, 1298 (Fed. Cir. 1999).

The Examiner's cite to MPEP 2145, section D and *In re Fulton*, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004) does not support the Examiner's position.

Unlike the present case (in which evidence shows that the direction taken by the glucose oxidase biosensor industry was a different direction than the claimed invention), the case of *In re Fulton* involved the selection of alternative shapes (square, triangle, hexagonal) for tread on the sole of a shoe. In the case of *In re Fulton*, the evidence did not show that the shoe industry was directed toward one shape and not others. In contrast, the evidence of record in the present application shows that those skilled in the art were addressing peroxide degradation by using additives and attached supports made of materials that deactivate peroxide. That direction of the industry is contrary to the invention recited in the present claims. Accordingly, the present application is distinguished from the facts in *In re Fulton*.

In addition, while the Examiner cited section D of MPEP 2145, it is noted that part 3 of that same section of the MPEP expressly deals with situations as in the present case, where the prior art and accepted wisdom in the art evidences nonobviousness of the present invention.

"The totality of the prior art must be considered, and proceeding contrary to accepted wisdom in the art is evidence of nonobviousness. *In re Hedges*, 783 F.2d 1038, 228 USPQ 685 (Fed. Cir. 1986) (Applicant's claimed process for sulfonating diphenyl sulfone at a temperature above 127°C was contrary to accepted wisdom because the prior art as a whole suggested using lower temperatures for optimum results as evidenced by charring, decomposition, or reduced yields at higher temperatures.)" MPEP 2145 D.3.

Thus, the Examiner's cite to section D of MPEP 2145, does not support the Examiner's argument. Instead, Section D.3. of the MPEP 2145 supports the patentability of the present claims, consistent with the positions expressed in Applicant's briefs. Also, because the present case is distinguished from the facts in *In re Fulton* (which did not involve evidence of a direction taken by the industry), the Examiner's cite to *In re Fulton* does not support the Examiner's argument. Accordingly, the Examiner has failed to establish a *prima facie* case of obviousness.

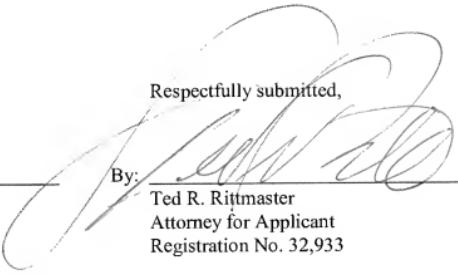
Next, the Examiner indicates that Applicant has argued against the references individually and that one cannot show nonobviousness by attaching references individually when the rejections are based on combinations of references. (Answer, pg. 12, l. 19 et seq.) Contrary to the Examiner's argument, Applicant has argued that Valdes et al. teach away from the claimed invention and, thus teach away from the Examiner's proposed combination of references (e.g., Applicant's Appeal Brief, pg. 10, ll. 12-14; and pg. 16, ll. 6-8). Applicant has further argued that Cherry et al. and Hatzinkolaou et al. do not address the distinctions between the claimed invention and the Valdes et al. reference (e.g., Applicant's Appeal Brief, pg. 10, l. 24 et seq.). In addition, Applicant has argued that it would not have been obvious to combine Cherry et al. with Valdes et al. because there is no logical relation between Cherry et al.'s clothes washing detergent (or the environment of a clothes wash cycle) and glucose oxidase enzymes for glucose sensors (e.g., Applicant's Appeal Brief, pg. 11, l. 26 to pg. 12, l. 15). Applicant has further argued that it would not have been obvious to combine Hatzinkolaou et al. with Valdes et al. or Cherry et al., because Hatzinkolaou et al.'s purpose of forming a library of a new simulated glucose osidase would have no applicable purpose in any mutation process described by Cherry et al. (e.g., Applicant's Appeal Brief, pg. 13, ll. 3-6). Thus, the Examiner's "response to appellant's arguments against the references individually" (Answer, beginning at pg. 12, l. 19) misses the points raised by the Applicant, with regard to the non-obviousness to combine the references in the manner proposed by the Examiner.

The Examiner has failed to show any reason or motivation that would have led one of ordinary skill in the art of making glucose biosensors, to look to the field of clothes washing detergents (as described by Cherry et al.), as an appropriate manner to modify (or replace) a process described by Valdes et al. for making an enzyme for a glucose biosensor.

The Examiner argues that Cherry et al. teaches a solution to the same problem disclosed by Valdes et al. (Answer, pg. 12, ll. 13-14.) But that is not the case. Cherry et al. is not involved with glucose oxidase or seeking a solution to peroxide degradation of glucose oxidase. Cherry et al. was, instead, concerned with producing a peroxidase for a clothes-washing detergent. That Cherry et al. was seeking a peroxidase that was resistant to H₂O₂ degradation during a washing cycle, would not have suggested that Cherry et al.'s process of making peroxidase for laundry detergent would be a solution to degradation of glucose oxidase enzymes in biosensors.

Accordingly, it is respectfully submitted that it would not have been obvious to combine the Cherry et al. and Hatzinikolaou et al. references with the Valdes et al. reference in the manner suggested by the Examiner. The Examiner's has not raised a *prima facie* case of obviousness. The rejections of claims 1, 3-8, 10-24 and 44-46 are, therefore, respectfully traversed and should be reversed.

Respectfully submitted,

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